

IT IS CLAIMED:

Sub B2
1. A stable liquid pharmaceutical botulinum toxin formulation, comprising
a pharmaceutically acceptable buffer capable of providing a buffered pH range
5 between about pH 5 and pH 6, and
isolated botulinum toxin;
wherein said formulation is stable as a liquid for at least one year at a temperature
between about 0 and 10 degrees centigrade.

Sub A1
2. The formulation of claim 1, wherein said temperature is about 5 ± 3 degrees
centigrade.

3. The formulation of claim 1, wherein said temperature is about 4 ± 2 degrees
centigrade.

4. The formulation of claim 1, wherein said buffered pH range is about $\text{pH } 5.6 \pm 0.2$.

5. The formulation of claim 1, wherein said toxin formulation is stable in liquid form
for at least two years.

6. The formulation of claim 1, wherein said buffer has a pK in the range of pH 4.5-
6.5.

7. The formulation of claim 6, wherein said buffer is selected from the group
consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

Sub A2
8. The formulation of claim 1, wherein said botulinum toxin is a botulinum toxin
serotype selected from the group consisting of serotypes A, B, C₁, C₂, D, E, F and G.

9. The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type
B present at a concentration in the range of about 100-20,000 U/ml.

10. The formulation of claim 9, wherein said botulinum toxin Type B is present in a high molecular weight complex of about 700 kilodaltons (kD).

5 11. The formulation of claim 9, wherein said botulinum toxin Type B is present at a concentration between about 1000-5000 U/ml.

12. The formulation of claim 8, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of about 20-2000 U/ml.

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13. The formulation of claim 12, wherein said botulinum toxin Type A is present at a concentration in the range of about 100-1000 U/ml.

14. The formulation of claim 1, which further includes an excipient protein.

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15. The formulation of claim 14, wherein said excipient protein is selected from the group consisting of serum albumin, recombinant human serum albumin, and gelatin.

16. A stable liquid pharmaceutical botulinum toxin formulation, comprising
a pharmaceutically acceptable liquid buffer capable of providing a buffered pH
range between about pH 5 and pH 6, and
isolated botulinum toxin,
wherein said toxin formulation is stable as a liquid for at least about 6 months at a
temperature between about 10 and 30 degrees centigrade.

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17. The formulation of claim 16, wherein said temperature is about 25°C.

18. The formulation of claim 16, wherein said buffered pH range is about pH
5.6±0.2.

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19. The formulation of claim 16, wherein said buffer has a pK in the range of pH 4.5-6.5.

20. The formulation of claim 19, wherein said buffer is selected from the group consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

Sub
A3 21. The formulation of claim 16, wherein said botulinum toxin is a botulinum toxin serotype selected from the group consisting of serotypes A, B, C₁, C₂, D, E, F and G.

10 22. The formulation of claim 21, wherein said botulinum toxin is botulinum toxin Type B present at a concentration of about 100-20,000 U/ml.

23. The formulation of claim 22, wherein said botulinum toxin Type B is present in a high molecular weight complex of about 700 kD.

15 24. The formulation of claim 22, wherein said botulinum toxin Type B is present at a concentration in the range of about 1000-5000 U/ml.

25 25. The formulation of claim 21, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of about 20-2000 U/ml.

26. The formulation of claim 25, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of about 100-1000 U/ml.

25 27. The formulation of claim 16, which further includes an excipient protein.

28. The formulation of claim 25, wherein said excipient protein is selected from the group consisting of serum albumin, human serum albumin, and gelatin.

30 29. A method of treating a patient in need of inhibition of cholinergic input to a selected muscle, muscle group, gland or organ, comprising

administering to the selected muscle, muscle group, gland or organ of the patient
a pharmaceutically effective dose of a liquid botulinum toxin formulation which
includes a pharmaceutically acceptable buffer capable of providing a buffered pH range
between about pH 5 and pH 6, and

5 isolated botulinum toxin;

wherein said toxin formulation is stable as a liquid for at least one year at a
temperature between about 0 and 10 degrees centigrade or for at least six months at a
temperature between about 10 and 30 degrees centigrade.

10 30. The method of claim 29, wherein said patient is suffering from a disorder
selected from the group consisting of spasticity, blepharospasm, strabismus, hemifacial
spasm, dystonia, otitis media, spastic colitis, anismus, urinary detrusor-sphincter
dyssynergia, jaw-clenching, and curvature of the spine.

15 31. The method of claim 30, wherein said patient is suffering from spasticity due to
one or more of the group consisting of stroke, spinal cord injury, closed head trauma,
cerebral palsy, multiple sclerosis, and Parkinson's disease.

20 32. The method of claim 30, wherein said patient is suffering from a dystonia
selected from the group consisting of spasmodic torticollis (cervical dystonia), spasmodic
dysphonia, limb dystonia, laryngeal dystonia, and oromandibular (Meige's) dystonia.

25 33. The method of claim 29, wherein said selected muscle or muscle group produces
a wrinkle or a furrowed brow.

34. The method of claim 29, wherein said muscle is a perineal muscle and wherein
said patient is in the process of giving birth to a child.

30 35. The method of claim 29, wherein said patient is suffering from a condition
selected from the group consisting of myofascial pain, headache associated with
migraine, vascular disturbances, neuralgia, neuropathy, arthritis pain, back pain,

hyperhydrosis, rhinorrhea, asthma, excessive salivation, and excessive stomach acid secretion.

36. The method of claim 29, wherein said formulation is stable as a liquid for at least
5 one year at a temperature of about 5 ± 3 degrees centigrade.

37. The method of claim 29, wherein said formulation is stable as a liquid for at least
one year at a temperature of about 4 ± 2 degrees centigrade.

10 38. The method of claim 29, wherein said formulation is stable as a liquid for at least
two years at a temperature between about 0 and 10 degrees centigrade.

39. The method of claim 29 wherein said buffered pH range is about pH 5.6 ± 0.2 .

15 40. The method of claim 29, wherein said buffer has a pK in the range of pH 4.5-6.5.

41. The method of claim 29, wherein said buffer is selected from the group
consisting of phosphate buffer, phosphate-citrate buffer, and succinate buffer.

20 42. The method of claim 29, wherein said botulinum toxin is a botulinum toxin
serotype selected from the group consisting of serotypes A, B, C₁, C₂, D, E, F and G.

43. The method of claim 42, wherein said botulinum toxin is botulinum toxin Type
B present at a concentration in the range of about 100-20,000 U/ml.

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44. The method of claim 43, wherein said botulinum toxin Type B is present in a
high molecular weight complex of about 700 kD.

45. The method of claim 43, wherein said botulinum toxin Type B is present at a
30 concentration between about 1000-5000 U/ml.

46. The method of claim 42, wherein said botulinum toxin is botulinum toxin Type A, present at a concentration in the range of about 20-2000 U/ml.

47. The method of claim 46, wherein said botulinum toxin Type A is present at a
5 concentration in the range of about 100-1000 U/ml.

48. The method of claim 29, which further includes an excipient protein.

49. The method of claim 48, wherein said excipient protein is selected from the
10 group consisting of serum albumin, recombinant human serum albumin, and gelatin.

50. The method of claim 29, wherein said patient is refractory to botulinum toxin
Type A and said botulinum toxin in said formulation is selected from the group
consisting of botulinum serotypes B, C₁, C₂, D, E, F and G.
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51. The method of claim 50, wherein said botulinum toxin in said formulation is
botulinum toxin Type B.

52. The method of claim 29, wherein said patient is refractory to botulinum toxin
20 Type B and said botulinum toxin in said formulation is selected from the group consisting
of botulinum serotypes A, C₁, C₂, D, E, F and G.

53. The method of claim 52, wherein said botulinum toxin in said formulation is
botulinum toxin Type A.
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